

بسم الله الرحمن الرحيم





شبكة المعلومات الجامعية التوثيق الالكتروني والميكرو فيلم



جامعة عين شمس

التوثيق الإلكتروني والميكرو فيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
على هذه الأقراص المدمجة قد أعدت دون أية تغييرات



يجب أن

تحتفظ هذه الأقراص المدمجة بعيدا عن الغبار





Effect of Ibuprofen Versus Acetaminophen On Postpartum Blood Pressure In Egyptian Women with Severe Preeclampsia: A Double-Blinded, Randomized Controlled Trial

Thesis

Submitted for partial fulfillment of the Master Degree in
Obstetrics and Gynecology

By

Zeinab Nabil Sayed Ahmed

M.B.B.CH, Ain Shams University 2014

Under Supervision of

Prof. Dr. Alaa El-Din Abd El-Aziz El-Guindy

Professor of Obstetrics & Gynecology
Faculty of Medicine, Ain Shams University

Dr. Mohammed Mahmoud El Sherbeny

Assistant Professor of Obstetrics & Gynecology
Faculty of Medicine, Ain Shams University

Dr. Radwa Mansour Mohamed Zaki

Assistant Professor of Obstetrics & Gynecology
Faculty of Medicine, Ain Shams University

**Faculty of Medicine
Ain Shams University
2021**

Effect of Ibuprofen versus Acetaminophen on Postpartum Blood Pressure in Egyptian Women with Severe Preeclampsia: A Double-Blinded, Randomized Controlled Trial

Zeinab Nabil Sayed Ahmed *, Alaa El-Din Abd El-Aziz El-Guindy **, Mohammed Mahmoud El Sherbeny ***, Radwa Mansour Mohamed Zaki ****

ABSTRACT

Objective: Generation of evidence for or against the use of nonsteroidal anti-inflammatory drugs in women with postpartum hypertension (HTN) and evaluation of the effect of ibuprofen versus acetaminophen on postpartum Blood pressure (BP) control among women with preeclampsia with severe features.

Methods: This double-blinded, randomized controlled trial included 150 severe preeclamptic pregnant women. All women were randomly allocated into two equal groups; group A: included 75 women and were given 500 mg acetaminophen and group B: included 75 women and were given 600 mg ibuprofen. They received either acetaminophen 500 mg or ibuprofen 600 mg within 6 hours after delivery for every 6 hours started immediately after delivery and continued for the duration of their postpartum hospitalization (72 hours).

Results: No significant differences were noted between women of both groups regarding antepartum and postpartum systolic or diastolic blood pressures. There were no significant differences between women of both groups regarding 10-cm VAS for postpartum pain and rates of moderate-to-severe pain in the first 24 hours and 24-48 hours postoperatively. Finally, there were no significant differences between women of both groups regarding rates of severe systolic or diastolic hypertension up to 48 hours postoperatively.

Conclusion: In women with severe preeclampsia, short term using - up to 48 hours - of NSAIDs as ibuprofen and acetaminophen for post cesarean section analgesia had no significant effect on maternal blood pressure.

Keywords: Ibuprofen, Acetaminophen, Postpartum Blood Pressure, Preeclampsia.



Acknowledgement

First of all, all gratitude is due to **Allah** almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.

Really I can hardly find the words to express my gratitude to **Prof. Dr. Alaa El-Din Abd El-Aziz El-Guindy**, Professor of Obstetrics & Gynecology, Faculty of Medicine, Ain Shams University, for his supervision, continuous help, encouragement throughout this work and tremendous effort he has done in the meticulous revision of the whole work. It is a great honor to work under his guidance and supervision.

I would like also to express my sincere appreciation and gratitude to **Dr. Mohammed Mahmoud El Sherbeny**, Assistant Professor of Obstetrics & Gynecology, Faculty of Medicine, Ain Shams University, for his continuous directions and support throughout the whole work.

I cannot forget the great help of **Dr. Radwa Mansour Mohamed Zaki**, Assistant Professor of Obstetrics & Gynecology, Faculty of Medicine, Ain Shams University for her invaluable efforts, tireless guidance and for her patience and support to get this work into light.

Last but not least, I dedicate this work to **my family**, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.



Zeinab Nabil Sayed Ahmed

List of Contents

	Page
Acknowledgment	--
List of Abbreviations	i
List of Figures	iii
List of Tables	iv
Introduction	1
Aim of The Work	3
Review of Literature	4
Chapter 1 : Preeclampsia	4
Chapter 2 : Pain management in postpartum period	51
Patients and Methods	78
Results	84
Discussion	94
Summary	103
Conclusion	106
Recommendations	107
References	108
Arabic Summary	--

List of Abbreviations

ACE	: Angiotensin converting enzyme
ACOG	: American College of Obstetricians and Gynecologists
ALT	: Alanine aminotransferase
ARBs	: Angiotensin II receptor blockers
AST	: Aspartate aminotransferase
B2	: Bradykinin
BMI	: Body mass index
BNP	: Brain Natriuretic Peptide
BP	: Blood pressure
CBC	: Complete blood count
CNS	: Central nervous system
COX	: Cyclooxygenase
CSF	: Cerebrospinal fluid
DIC	: Disseminated intravascular coagulation
ESRD	: End-stage renal disease
FDA	: Food and Drug Administration
Flt-1	: the full-length VEGF receptor type-1
GABA	: Gamma-aminobutyric acid
HOT	: Hypertension Optimal Treatment
HTN	: Hypertension
ICU	: Intensive care unit
IM	: Intramuscular
IQR	: Inter quantile range
IV	: Intravenous
LDH	: Lactate dehydrogenase
MRAs	: Mineralocorticoid receptor antagonists
UNICEF	: United Nations Children's Emergency Fund
NMDA	: N-methyl-D-aspartate
NO	: Nitric oxide

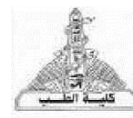
NSAIDs	: Nonsteroidal antiinflammatory drugs
PCA	: Patient-controlled analgesia
PlGF	: Placental growth factor
PONV	: Postoperative nausea and vomiting
PROM	: Prelabour rupture of the membranes
RR	: Relative risk
SD	: Standard Deviation
sFlt-1	: Placental Soluble Fms-Like Tyrosine Kinase 1
sEng	: Soluble endoglin
SPSS	: Statistical program for social science
USPSTF	: The US Preventive Services Task Force
VAS	: Visual Analogue Scale
VEGF	: Vascular endothelial growth factor

List of Figures

Fig.	Title	Page
1	Bar-Chart showing Difference between Groups regarding Rates of Moderate-to-Severe Pain within 48 hours Postoperatively.	87
2	Bar-Chart showing Difference between Groups regarding Rates of severe systolic or diastolic hypertension up to 48 hours postoperatively.	
3	Bar-Chart showing Difference between Groups regarding Need for Extra Analgesia.	88
4	Bar-Chart showing Difference between Groups regarding Need for Opioid Analgesia.	89
5	Curve-Chart showing Difference between Groups regarding Postpartum Systolic Blood Pressure.	91
6	Curve-Chart showing Difference between Groups regarding Postpartum Diastolic Blood Pressure.	91
7	Bar-Chart showing Difference between Groups regarding Inpatient Anti-Hypertensive Medications.	92
8	Bar-Chart showing Difference between Groups regarding Outpatient Anti-Hypertensive Medications.	92
9	Bar-Chart showing Difference between Groups regarding Need for Anti-Hypertensive Treatment 6 weeks Postpartum.	93

List of Tables

Table	Title	Page
1	Difference between Groups regarding Demographic Characteristics.	84
2	Difference between Groups regarding Antepartum Data.	85
3	Difference between Groups regarding Delivery and Postpartum Data.	86
4	Difference between Groups regarding Postpartum Pain.	87
5	Difference between Groups regarding Rates of Severe Hypertension within 48 hours Postoperatively.	90



PROTOCOL OF A THESIS FOR PARTIAL FULFILMENT OF MASTER DEGREE IN OBSTETRICS & GYNECOLOGY

Title of the Protocol:

**Effect of ibuprofen versus acetaminophen on
postpartum blood pressure in Egyptian women with
severe preeclampsia: a double-blinded, randomized
controlled trial**

Postgraduate Student: Zeinab Nabil Sayed Ahmed

M.B.B.CH, Ain Shams University 2014

DIRECTOR: Prof. Alaa El-Din Abd El-Aziz El-Guindy

Academic Position: Professor

Department: Obstetrics & Gynecology, Faculty of Medicine, Ain Shams
University

Co-DIRECTOR: Dr. Mohammed Mahmoud El Sherbeny

Academic Position: Assistant Professor

Department: Obstetrics & Gynecology, Faculty of Medicine, Ain Shams
University

Co-DIRECTOR: Dr. Radwa Mansour Mohamed Zaki

Academic Position: Lecturer

Department: Obstetrics & Gynecology, Faculty of Medicine, Ain Shams
University

**Faculty of Medicine
Ain Shams University
2018**

What is already known on this subject? AND What does this study add?

There is a hypothesis that nonsteroidal anti-inflammatory drugs use would adversely affect postpartum blood pressure control in women with preeclampsia however evidence to support this is lacking.

1. INTRODUCTION

Hypertensive disorders are important contributors to maternal morbidity and mortality, and women diagnosed with a hypertensive disorder of pregnancy are likely to meet criteria for postpartum antihypertensive therapy as well as require several days of postpartum observation (*Sharma et al., 2017; Viteri et al., 2017*). In addition, women with hypertensive disorders of pregnancy are at increased risk for cesarean delivery, with its attendant need for postoperative pain relief (*Kim et al., 2010*).

Chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs), particularly cyclooxygenase inhibitors, is known to increase the risk of development of hypertension (HTN) in healthy, nonpregnant women as well as to antagonize the effects of some antihypertensive drugs in hypertensive patients receiving treatment after just a few days of NSAID use (*Floor-Schreudering et al., 2015*). The hypothesized mechanisms for this effect include the NSAID-mediated alteration of aldosterone metabolism, (*Knights et al., 2006*) sodium retention, inhibition of prostaglandin-mediated vasodilation, and production of vasoactive metabolites of arachidonic acid via cytochrome-P450 induction (*Blue et al., 2018*).

Because of this concern, the American College of Obstetricians and Gynecologists (ACOG) suggests avoiding the postpartum use of NSAIDs in women diagnosed with preeclampsia who have postpartum hypertension (HTN), though evidence in support of this recommendation is limited (*ACOG, 2013*). Animal studies are limited to a single investigation in a rat model of preeclampsia, which showed that indomethacin had no effect on blood pressure (BP) while rats were still pregnant. In human beings, the limited data on the influence of NSAIDs on postpartum BP among women with preeclampsia are conflicting (*Vigil-De Gracia et al., 2017*).

NSAIDs are ideally suited for postpartum pain control and are still widely used for postpartum and postcesarean delivery pain management in nonhypertensive women because of their effectiveness (*Sammour et al., 2011*). They are more effective than acetaminophen

to alleviate pain from obstetric perineal injury, and have also been shown to decrease opioid use after cesarean delivery (*Deussen et al., 2011*).

Additionally, the analgesic alternatives to cyclooxygenase inhibitors have significant risks. The use of postpartum opioids may predispose to ongoing opioid dependence and is associated with neonatal central nervous system depression during breast-feeding. Although acetaminophen is an additional nonopioid alternative that may decrease the use of postcesarean opioids, its use is contraindicated in the setting of severe, acute elevation of liver enzymes, a common occurrence among patients with severe variants of preeclampsia (*Towers et al., 2018*).

It remains unclear whether the theoretical adverse effect of short-term NSAID use on postpartum BP is clinically significant and justifies for going their analgesic properties (*Blue et al., 2018*).

2. AIM/ OBJECTIVES

The aim of this study is to generate evidence for or against the use of nonsteroidal anti-inflammatory drugs in women with postpartum hypertension (HTN).

We will conduct this study to evaluate the effect of ibuprofen vs acetaminophen on postpartum BP control among women with preeclampsia with severe features.

3. METHODOLOGY:

Patients and Methods

- **Study design:** A double-blinded, randomized controlled trial
- **Study setting:** The study will be conducted at Ain Shams University Maternity Hospital.
- **Inclusion criteria:**
Severe preeclampsic pregnant women who are:
 - Age ≥ 18 years old
 - Preeclampsia with severe features:
 - SBP ≥ 140 mmHg or DBP ≥ 90 mmHg.
 - Impaired liver function: elevated liver enzyme but < 200 mg/dL,

- Evidence of kidney dysfunction (serum creatinine concentration < 1.0 mg/dL)
- New onset of visual disturbances.
- Thrombocytopenia but with platelet count >100,000 / μ L (*American College of Obstetricians and Gynecologists, 2013*).
- Chronic HTN with super-imposed preeclampsia with severe features.
- Acceptance to participate in the study (written consent)
- **Exclusion criteria:**
 - Alanine aminotransferase (ALT) > 200 mg/dL (*Blue et al., 2018*).
 - Aspartate aminotransferase (AST) >200 mg/dL (*Blue et al., 2018*).
 - Serum creatinine >1.0 mg/dL
 - Chronic kidney disease
 - Chronic liver disease
 - Gastroesophageal reflux disease
 - peptic ulcer disease
 - Bleeding disorder
 - Known sensitivity or allergy to NSAIDs or acetaminophen
- **Study population:**

The study will include 150 preeclamptic pregnant women attending pre-labor room. All women will be randomly allocated into two groups as follows:

 - **Group A:** including 75 women and will be given 500 mg acetaminophen. (Manufactured by Alexandria Co. For Pharmaceuticals & Chemical Industries). M.O.H.Reg.No.27330 / 2011
 - **Group B:** including 75 women and will be given 600 mg ibuprofen. (Manufactured by Kahira Co. For Pharmaceuticals & Chemical Industries). M.O.H.Reg.No.16927 / 2015

They will receive either acetaminophen 500 mg or ibuprofen 600 mg within 6 hours after delivery for every 6 hours starting immediately after delivery and continuing for the duration of their postpartum hospitalization (72 hours).